overnight in DMEM supplemented with 10% FBS and 20 mU/ml insulin. On the following day, cells were transfected with an expression pAdTRACKCMV- $LDLR_{KDEL}$ for a fusion protein of the LDLR truncated receptor with the KDEL localization domain, or $LDLR_{KDEL}$, or with a control plasmid. The transfections were performed using the TransIT-Insecta transfection reagent (Mirus) following the manufacturer's protocol, except that the transfections were performed using 10 μg DNA and 40 μl TranIT-Insecta reagent per 2 ml supplemented with DMEM and 10% FBS in a 60 mm dish of cultured hepatocytes. Transfected hepatocytes were cultured for an additional 36-48 hour period prior to further experimentation.--

Page 7, paragraph beginning line 3, please substitute the following:

--Labeling. The hepatocytes were incubated for 1 hour in starve medium before pulse-labeling for 7.5 minutes with radioactive tracer (200 μCi [^{35}S] methionine/cysteine/60 mm dish). The dishes were washed one time with DMEM prior to addition of chase medium (DMEM supplemented with 10mM each of labeled methionine and cysteine and 0.2 mM oleic acid).--

Page 7, paragraph beginning line 8, please substitute the following:

--Immunoprecipitation. Following the radiolabeling, the media were collected and centrifuged (5 min., 1000 rpm). The resulting media were used for immunoprecipitations. Cells were rinsed three times with ice-cold PBS, scraped into PBS, and collected by centrifugation. The cell pellets were lysed in 200 μl RIPA/1% SDS (150 mM NaCl; 50 mM Tris (pH 7.5); 1% Triton X-100; 0.5% deoxycholate; 1% SDS; 1mM PMSF; 1 mM orthovanadate; 10 μg/ml trypsin inhibitor; 10 μg/ml leupeptin). The mixture was then diluted five times to 1 ml final volume in 150 mM NaCl; 50 mM Tris (pH 7.4); 1 mM PMSF; 1 mM orthovanadate; 10 mg/ml trypsin inhibitor; 10 mg/ml leupeptin. For immunoprecipitations, both the media and the cell lysates were supplemented with 1/5 volume IMB (100 mM Tris (pH 7.4), 25 mM EDTA, 5 mg/ml BSA; 2.5% sodium deoxycholate, 2.5% Triton X-100, 0.01% sodium azide). Antibodies to apoB (polyclonal, rabbit anti-pig LDL) or albumin (polyclonal, rabbit anti-human serum albumin; Sigma) were also added. For the precipitations of albumin, IMB did not contain BSA. After an overnight incubation at 4°C, Protein A-agarose beads (Gibco-BRL) were added and the incubation continued at 4°C overnight. The antibody/ bead slurry was subsequently washed, once with PBB (10 mM phosphate buffer (pH 7.4), 1 mg/ml BSA, 0.01% sodium azide) and once with PB (PBB

without BSA). Radiolabeled protein was solubilized in SDS-sample buffer (2% SDS, 20% glycerol, 50mM Tris (pH 6.8), 6 M urea, 1 mM EDTA, 20 mg/ml bromophenol blue), supplemented with 10 mM DTT and 250 mM β-mercaptoethanol, and heated at 65°C for 30 minutes prior to SDS polyacrylamide gel electrophoresis (SDS-PAGE). Specific proteins were visualized by autoradiography and the amounts on unlabeled protein were determined by storage phosphor technology (PhosphorImager, Molecular Dynamics; ImageQuant version 3.3). All data was normalized to cellular protein and total TCA-precipitable radiation.--

Page 8, paragraph beginning line 11, please substitute the following:

--In a first trial, plasmids encoding either $LDLR_{KDEL}$ or β-galactosidase (control) were injected into a tail vein of mice lacking a functional LDL receptor. Approximately 48 hours after the injection, the mice were fasted for 4 hours and then sacrificed. Plasma from the mice was harvested, diluted 1:1 with PBS, filtered and fractionated using a Pharmacia Sepharose 6 column. The protein profile from that analysis is illustrated in Fig. 1. In Fig. 1, the VLDL/chylomicron remnant, LDL and HDL peaks are identified. Traces are representative for three animals for the control and two for the experimentals. The third experimental animal exhibited no change. Strikingly, the animal with the highest $LDLR_{KDEL}$ expression level, as determined by Western blot analysis, showed an about 50% reduction in plasma cholesterol levels (245.8 mg/dl before injection and 124.6 mg/dl after). Cholesterol levels showed little or no change in plasma from control animals.--

Page 8, paragraph beginning line 23, please substitute the following:

--The second trial using the $LDLR_{KDEL}$ vector *in vivo* was performed in mice which possessed a wild-type LDL receptor. In this trial the control selected was a plasmid encoding a protein that differs from the KDEL motif by a single amino acid substitution (Ile (140) to Asp). This variant, designated KDEL-ID, was predicted to be deficient in apoB binding and appeared from *in vitro* experimentation to be a suitable control. Mice were injected in a tail vein with 25 μg of DNA coding for either $LDLR_{KDEL}$ or the KDEL-ID variant. Experiments were performed using the Trans-IT In Vivo protocol (Mirus Corporation) according to the manufacturer's instructions. Plasma was harvested approximately 48 hours after injection following a 4 hour fast. The recovered plasma was diluted 1:1 with PBS, filtered and lipoprotein particles were separated on a Sepharose 6 gel filtration FPLC column (Pharmacia). Cholesterol values for each fraction were determined enzymatically (Sigma). The data is shown in Fig. 2, which represents the mean values for three animals for each